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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/739,933	12/18/2000	James Steven Reid	E8019-00001	4882

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EXAMINER	
MACFARLANE, STACEY NEE	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/739,933	REID ET AL.	
	Examiner	Art Unit	
	STACEY MACFARLANE	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8,33,63-66 and 70-73* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 5-8, 33, 63-66 and 70-73* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/28/2010*.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 1, 5, 33, 63, 65, 66 and 70 have been amended, claims 71-73 have been newly added as requested in the amendment filed on February 26, 2010. Following the amendment, claims 1, 2, 5-8, 33, 63-66 and 70-73 are pending in the instant application.

Claims 1, 2, 5-8, 33, 63-66 and 70-73 are under examination in the instant office action.

Priority

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See Transco Products, Inc. v. Performance Contracting, Inc., 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, provisional Application No. 60/055,383 (hereafter '383), fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this

application. The '383 application fails to disclose the sequence $CX_7CX_4CX_{10}CXCX_8C$ (SEQ ID NO: 1). Since, as currently amended, pending claims 1, 2, 5-8, 33, 63-66 and 70-72 include this limitation, and will be given the effective filing date of August 4, 1998, which is the filing date of Application No. 09/129,028 in which the sequence is first disclosed (page 28 of the specification). Claim 73 is limited to the administration of the polypeptide TGF-α, not the fragment comprising the sequence, and will be given the benefit of the filing date of the provisional application, August 4, 1997.

Claim Rejections - 35 USC § 112 (Withdrawn)

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. The rejection of Claims 1, 2, 5-8, 33 and 63-64 under 35 U.S.C. 112, first paragraph, lack of written description for the "functional fragment" of the claims, is withdrawn in light of the claim amendments providing a core structure (SEQ ID NO:1) to said claimed fragments.

5. In view of the current amendments and the arguments presented in Remarks filed August 8, 2008, the rejection of Claims 1, 2, 5-8, 33 and 63-64 under 35 U.S.C. 112, first paragraph, scope of enablement, is withdrawn.

Claim Rejections - 35 USC § 102 (Withdrawn)

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

7. The rejection of Claim 73 under 35 U.S.C. 102(a) as being anticipated by Alexi et al., *Neuroscience*, 78(1):73-86, published May, 1997, has been withdrawn in view of the Declaration of James Fallon under 37 CFR § 1.131 filed on December 2, 2002, which demonstrates evidence that the claimed invention was conceived March 1997.

Claim Rejections - 35 USC § 102 (New Grounds)

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

As currently amended, Claims 1, 2, 5-7, 33, 63-64 and 70-72 are rejected under 35 U.S.C. 102(b) as being anticipated Alexi et al., *Neuroscience*, 78(1):73-86, published May, 1997, as applied to claims 1, 2, 5-7, 33, 63-64 for reasons of record in the previous Office action. It should be noted that, as stated in section 2 above, the benefit of Priority has been amended and the reference serves as prior art published more than one year prior to the effective date of the amended claims.

Claim Rejections - 35 USC § 103 (New Grounds)

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

11. Claims 1, 2, 5-8, 33, 63-66 and 70-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weiss et al. US Patent 5,980,885 filed June 7, 1995 and issued November 9, 1999 (cited in Office action mailed 8/5/2002), in view of Kelly et al., Brain Research, 94(3): 507-522, September 5, 1974.

The instant claims recite delivery of TGF-α polypeptide or functional fragment thereof "outside of the ventricles" to the striatum, pallidum, septum, cortex, external capsule, internal capsule, substantia nigra-ventral tegmentum or at or adjacent to an ependymal or subependymal zone.

Weiss et al., teaches a method for treating neurodegenerative disease comprising stimulating in vivo mammalian neural stem cell proliferation and differentiation comprising administering TGF-α. The Weiss Patent teaches that

administration of the growth factors can be done by any method known in the art at the time of filing, "including injection cannula, transfection of cells with growth hormone-expressing vectors, injection, and timed release apparati which can administer substances at the desired site" (Column 25, lines 40-column 26, line 15). Such sites include transplantation to basal gangia, caudate, putamen, nucleus basalis or substantia nigra, or striatum (column 23, lines 4-21). The Weiss Patent explicitly contemplates administration at the site of damage or lesion where promotion of proliferation and differentiation of neural stem cell progeny occurs, such as in Parkinson's Disease where treatment occurs in the substantial nigra (Column 60) or treatment of ischemic injury or stroke (column 61) at lesions within the caudal striatum and parietal cortex. Additionally, the mechanism of action for the Weiss Patent is that the invention provides a means for generating large numbers of undifferentiated and differentiated neural cells in vivo, arising from the ependymal zone as required by instant claim 72(Column 13 lines 21-41), for the treatment of neurodegenerative disease and trauma (Column 11, lines 40-66). The art at the time of filing recognized that these neural stem cells migrate within the CNS. The Weiss Patent explicitly teaches that these neural stem cells undergo "a period of cell type differentiation and migration when undifferentiated progenitor cells differentiate into neuroblasts and gliolblasts [*sic*] which give rise to neurons and glial cells which migrate to their final positions" (paragraph bridging Columns 1 and 2). Additionally the Weiss Patent teaches, "neural stem cell progeny can migrate into regions that have been damaged as a result of injury or disease" (Column 26, lines 10-12). The Patent teaches suitable areas of interest for

treatment include those encompassed by the instant claims (Column 12, line 56-Column 13, line 8). Specifically, Weiss et al. teach continuous administration of growth factor for six days (Example 27) but demonstrate that longer periods of growth factor treatment (up to 21 days in vitro) predictably lead to additional increases in neural progenitor cell proliferation, differentiation and migration (Columns 35-37, Examples 8 and 9). The in vivo methods explicitly provide for treatment 7 days after the lesion (Column 20). Thus, the method as taught by Weiss encompass the limitations of the instant claims: continuous infusion (claim 64); growth factor treatment for a period of "at least about sixteen days" (claim 65); and treatment initiated at least 1 week after injury (claim 66).

While the Weiss Patent explicitly teaches TGF-α may be administered in vivo by any method known in the art at the time of filing, it does not explicitly disclose methods for delivery of TGF-α "outside of the ventricles", namely within the "striatum, pallidum, septum, cortex, external capsule, internal capsule, substantia nigra-ventral tegmentum or at or adjacent to an ependymal or subependymal zone" of the instant claims. However, such limitations are rendered obvious by the evidence that means for delivery outside the ventricles, such as within the striatum, were well-known in the art at the time of filing. The Kelly et al. prior art is relied upon as evidence that methods comprising direct intrastriatal injection via stereotaxic coordinates were well-recognized within the prior art.

It would have been obvious to one of ordinary skill in the art to use the methods of intrastriatal injection, as taught by Kelly et al., in the method as taught by the Weiss Patent. A skilled artisan would be motivated to combine the prior art elements because

combination would result in the intrastriatal delivery of TGF-α. In *KSR International Co. v. Teleflex, Inc.,* the Supreme Court has stated that combining prior art elements according to known method to yield predictable results is *prima facie* obvious if the following rationale can be applied:

> (1) the prior art includes each element claimed though not necessarily in the same reference.
> (2) it was within the technical grasp of one of ordinary skill in the art to combine the elements as claimed by known methods, and that in combination, each element merely would have performed the same function as it did separately.
> (3) one of ordinary skill in the art would have recognized that the results of such combination were predictable.

(KSR International Co. v. Teleflex, Inc. 127 S. Ct. 1727, 82 USPQ2d 1385, Supreme Court, April 30, 2007). Based on the guidance and direction within the prior art, such combination would have been well within the technical grasp of the skilled artisan. Since each of the elements (methods comprising in vivo administration of TGF-α and methods for intrastriatal delivery) in combination are merely performing the same function as they did separately, then one of ordinary skill in the art would have been able to predictably combine the elements with a reasonable expectation of success. Therefore, the invention as a whole is *prima facie* obvious.

Double Patenting

12. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory

obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

13. Claims 1, 5, 6, 33, 63, 65 and 70-73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 45, 48, 55 and 57-60 of copending Application No. 09/129,028. Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims of the '028 Application are drawn to treatment of neurological disorders

comprising intrastriatal delivery of TGF-α, which overlaps in scope with the methods of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims 1, 5, 6, 33, 63, 65 and 70-73 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3, 12-13, 41, 43, 53, 54 and 61-65 of copending Application No. 10/167,384. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are drawn to methods comprising delivery of TGF- α outside the ventricles, which overlaps in scope with the claims of the '384 Application drawn to methods comprising delivery outside the CNS.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

15. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to STACEY MACFARLANE whose telephone number is (571)270-3057. The examiner can normally be reached on M-R 5:45 to 3:30, TELEWORK-Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

/Daniel E. Kolker/
Primary Examiner, Art Unit 1649
May 28, 2010